Version with markings to show changes made

[0008] Benzamycin® (generic name: benzoyl peroxide and erythromycin topical; Dermik Lab.) is a topical gel for the treatment of acne comprising a combination of 3% erythromycin, as a topical antibiotic, and 5% benzoyl peroxide, as an antibacterial, keratolytic and desquamating agent. This combination, however, is unstable at room temperature for the above reason, so that Benzamycin®. rapidly loses its pharmaceutical effectiveness if stored at ambient temperature.

[0010] Various attempts have been made to overcome the instability of formulations such as Benzamycin®. U.S. Pat. No. 5,446,028, U.S. Pat. No. 5,767,098 and U.S. Pat. No. 6,013,637, for instance, disclose formulations further comprising a stabilising agent such as dioctyl sodium sulfosuccinate. U.S. Pat. No. 5,466,446 discloses a method for preparing a reportedly stable formulation comprising clindamycin and benzoyl peroxide by controlling the ratio of each active ingredient. The proprietor of this patent markets a product under the name Clindoxyl® Gel (generic name: clindamycin phosphate and benzoyl peroxide) which contains benzoyl peroxide and clindamycin in the ratio of 5:1 and which has a shelf-life of 60 days at room temperature. The product is, however, required to be kept refrigerated prior to being dispensed, which is inconvenient as well as impractical.

[0012] Benzaclin® (generic Name: benzoyl peroxide and clindamycin topical) is the only FDA-approved combination of 1% clindamycin phosphate and 5% benzoyl peroxide gel. Although this can be stored at room temperature (up to 25°C), this is only stable for about two months.

[0050] Polymeric delivery systems useful in products of the invention will generally comprise a polymer or polymers in the form of particles (e.g. microparticles), aggregates of particles (e.g. aggregates of microparticles) or clusters of aggregates (agglomerates) of particles (e.g. agglomerates of microparticles) which are capable of entrapping any desired active for delayed release. The polymer particles will generally be porous (i.e. these have an open structure) and will also typically be cross-linked, e.g. comprising a porous polymeric matrix. Examples of polymeric delivery systems suitable for use in the invention include the Poly-Trap® (INCI Name: Lauryl Methacrylate/ Dimethacrylate Crosspolymer~~Cardinal Health, Inc.~~) and Poly-Pore® (Allyl Methacrylate Crosspolymer~~Amcol International, Inc.~~) both commercially-available from Amcol Health and Beauty Solutions, Inc., and, in particular, the Microsponge® system as described below.~~(Advanced Polymer Systems, Inc.)~~.

[0067] The carriers may, for example, include conventional formulating ingredients selected from lipophilic base materials (for example fatty (e.g. C_{10-30}) alcohol esters of saturated or unsaturated fatty (e.g. C_{10-30}) acids, such as cetyl ricinoleate; fatty acid esters of sterols such as cholesterol or lanosterol; emollient silicon oils, e.g. polysiloxanes such as dimethicone or cyclomethicone; or terpenes such as .alpha.-bisabolol), hydrophilic base materials (for example polyethylene glycols, hereinafter referred to as PEGs), stabilisers and/or surfactants (for example fatty acids such as palmitic or stearic acid; fatty alcohols such as cetyl or stearyl alcohol; amphiphilic fatty esters, e.g. fatty alcohol esters of mineral acids such as sodium lauryl sulphate, fatty acid esters of polyols such as glyceryl dilaurate or caprylic/capric triglyceride; PEGylated fatty alcohols, e.g. PEG lauryl ethers such as laureth-4; PEGylated sorbitan esters with fatty acids such as oleic, lauric, palmitic or stearic acid~~, e.g. as in Tween® surfactants~~;

PEGylated sterols such as PEG-10 soya sterol; polysaccharides such as xanthan gum; is proprietary products such as emulsifying wax; or thickening polymeric stabilisers, ~~e.g. polyacrylamide-based products such as Sepigels®),~~ humectants (for example diols or polyols such as propylene glycol or glycerol), viscosity modifiers (for example saccharides such as sorbitol), thickeners (for example colloidal or fumed silica or silicates such as magnesium aluminium silicate), preservatives (for example antimicrobials or antifungals such as methyl paraben, propyl paraben, benzyl alcohol, or phenoxyethanol ~~or germaben II~~; or antioxidants such as vitamin E, ascorbyl palmitate or butylated hydroxytoluene), pH regulators (for example buffers, e.g. acid/salt combinations such as citric acid/sodium citrate; or bases such as triethanolamine), or anticoagulants (for example disodium edetate).

III. Remarks

No new matter is added by the amendments. Support for New Claims 33 – 35 is found at least in Paragraph [0068]. Support for New Claims 31 and 32 is found in at least Paragraph [0069]. Support for currently-amended Claim 10 is found at least in Paragraph [0047].

As requested in the Office Action, the Specification is amended to provide generic names for products otherwise referred to by their registered trademarks.

A. The Office Action Fails Make a *Prima Facie* Case of Obviousness

An obviousness determination requires "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *See, In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis added). *Accord, CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974))("obviousness requires a suggestion of all limitations in a claim.")

Each of the pending claims requires first and second active ingredient-containing formulations comprised of "water-based carrier bases having substantially the same lipophilicity." As set out in Paragraphs 7 – 11 of the 1.132 Declaration of Dr. Katz, WO 93/15726 ("WO26") – the primary reference that forms the basis for all of the pending rejections – does not teach or suggest creating a combination formulation made up of two components, where each of the components has substantially the same lipophilicity.

In the first full sentence on Page 3 of the Office Action, the absence of the required claim element "having substantially the same lipophilicity" is expressly noted. However, the Office Action concludes, without articulating a reasoned basis, that "the two compositions of the two components (table 1) are both water based and do not appear to vary in their hydrophilicity or lipophicility" (emphasis added). Applicants respectfully submit that such a conclusion is insufficient as a matter of law to support a finding of obviousness. In discussing the obviousness standard in *KSR Int'l v. Teleflex Inc.*, the Supreme Court explains "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added)).

Both Dr. Katz and Dr. Lochhead reach a different conclusion – namely that WO26 teaches two component formulations with widely disparate lipophilicities. In contrast to the Office Action, Dr. Katz articulates in considerable detail the scientific bases on which both he and Dr. Lochhead conclude that the benzoyl peroxide suspensions taught in WO26 do not have substantially the same lipophilicity as the clindamycin suspensions taught in WO26. *See* Katz Declaration at Paragraphs 7 – 11.

Applicants respectfully note that Claims 24 and 29 – 32 each have a further limitation with respect to the viscosity. Claim 24 expressly requires that the first and second formulations have substantially the same viscosity. Claims 29 – 32 are directed to a final combination product (made up of two components) having a specific viscosity – less than about 40,000 cps, less than about 30,000 cps, less than about 20,000 cps and less than about 10,000 cps.

In Paragraph 16 of his Declaration, Dr. Katz explains WO26 why does not teach two compositions having substantially the same viscosity. His explanation elaborates on and provides additional reasons that support the same conclusion reached by Dr. Lochhead. *See* Lochhead Declaration at Paragraph 27. Moreover, as explained by Dr. Katz in Paragraphs 14 – 16 of his declaration, neither WO26 nor the secondary references combined with WO26 teach or suggest a final formulation having the claimed viscosities.

Applicants respectfully submit that the Office Action fails to explain where cited references disclose or suggest the recited viscosity claim limitations. Applicants also respectfully submit that the Office Action does not provide a clearly-articulated rationale explaining why a person having ordinary skill in the viewing the cited references would have considered it obvious to modify the product combination benzoyl peroxide / clindamycin taught in WO26 in a manner such that the resulting finished product would have a viscosity of less than about 40,000 cps, less than about 30,000 cps, less than about 20,000 cps or less than about 10,000 cps.

In addition Applicants respectfully submit that the cited references do not provide a teaching, suggestion or motivation to replace the carboxyvinyl polymers taught in WO26 with a polymeric delivery system of the type claimed by the Applicants. The example benzoyl peroxide suspensions taught on page 12 of WO26 contain carboxyvinyl polymers. In Paragraphs 12 – 13 of his declaration, Dr. Katz explains that carboxyvinyl polymers are <u>not</u> "polymeric delivery systems". Dr. Lochhead provides a similar explanation in Paragraph 11 of his declaration. Applicants respectfully submit that the Office Action does not provide a clearly-articulated rationale explaining why a person having ordinary skill in the viewing the cited references would have considered it obvious

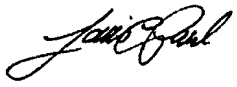
to modify the product combination benzoyl peroxide / clindamycin taught in WO26 by substituting a polymeric delivery system of the type claimed by the Applicants with a carboxyvinyl polymer as taught in WO26.

Conclusion

In summary, Applicants respectfully submit that in rejecting Claims 1 – 14, 16 – 26, 29 and 30 the Office Action fails to consider all claim limitations, a well-settled requirement of the patent law. *See In re Wada and Murphy,* Appeal 2007-3733 at page 8 (Board of Patent Appeals and Interferences, January 14, 2008) (quoting *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994) "[T]he Patent and Trademark Office (PTO) must consider all claim limitations when determining patentability of an invention over the prior art.") .

For the above reasons, it is respectfully submitted that the claims as presented are in condition for allowance. Favorable action is therefore earnestly solicited.
If the Examiner believes that an interview will expedite allowance, please contact undersigned counsel.

Respectfully submitted,



Dated: June 27, 2008

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